

Unveiling chronic lead toxicity: A case study on diagnosis, treatment, and recovery

İdris Baydar¹ 

¹ Mardin Artuklu University, Faculty of Medicine, Department of Internal Medicine, Mardin, Türkiye

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Correspondence:

Dr. İdris BAYDAR

Mardin Artuklu University, Faculty of
Medicine, Department of Internal Medicine,
Mardin, Türkiye.

E-mail: idrisbaydar@gmail.com



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Abstract

This case report presents the diagnostic challenges and successful management of chronic lead toxicity in a 31-year-old female with persistent nonspecific symptoms, including fatigue, cognitive dysfunction, and constitutional complaints. Despite comprehensive prior evaluations showing only mildly elevated inflammatory markers, a definitive diagnosis was achieved through DMSA-provoked urinary lead testing, revealing an approximately 80-fold increase from baseline (1.1 to 85.3 µg/g creatinine). The patient underwent a 3-month DMSA chelation regimen (30 mg/kg/day in 5-day cycles with 9-day intervals), resulting in a significant reduction of provoked lead levels to 11.3 µg/g creatinine and resolution of clinical symptoms. The case highlights three critical aspects of heavy metal toxicity: (1) the limitations of conventional testing in chronic low-level exposure, (2) the diagnostic utility of provoked urinary metal analysis, and (3) the therapeutic efficacy of oral DMSA chelation. This report emphasizes the importance of considering heavy metal toxicity in refractory cases of multisystem complaints and demonstrates the value of protocol-based diagnostic provocation testing in occult exposure scenarios. The favorable outcomes support DMSA as both a diagnostic and therapeutic agent for lead toxicity, suggesting that there should be standardized guidelines for interpreting provoked testing.

Keywords: Lead toxicity, DMSA provocation test, chelation therapy, cognitive dysfunction, constitutional complaints

Introduction

Heavy metal exposure is a significant concern in the modern age, as these metals are utilized across diverse sectors, including food, agriculture, construction, textiles, health, and technology. Even at low doses, some heavy metals exhibit substantial toxicity (1-6). Over time, environmental accumulation increases exposure risks for plants, animals, and humans, occurring via inhalation, ingestion, or dermal contact (2, 4, 6).

Lead represents a critical heavy metal exposure. It is extensively used in industries such as shipbuilding, paint production, battery manufacturing, agriculture, and pipe production. Lead contamination can also originate from gasoline, pottery, municipal water lines, paints, plastic containers, straws, medications, Ayurvedic products, food packaging, and toys (7-10).

Lead poisoning can affect both children and adults, causing damage to multiple organ systems. While neurological symptoms predominate, other manifestations include renal impairment, anemia, gastrointestinal disturbances, psychiatric issues, and dermatological symptoms (11). Acute or occupational exposure may facilitate diagnosis, whereas chronic, low-to-moderate exposures often present a diagnostic challenge due to nonspecific clinical features (2, 11, 12).

Various diagnostic methods have been described. Blood lead levels indicate circulating lead but do not reflect the total body burden, as lead predominantly accumulates in tissues such as bone (13). Techniques such as X-ray fluorescence can quantify lead in bones but are not routinely used due to technological limitations, the inability to assess total exposure, and the absence of standardized reference ranges (14, 15).

Urinary lead measurements following chelation provocation with agents such as dimercaptosuccinic acid (DMSA) or ethylenediaminetetraacetic acid (EDTA) offer an alternative diagnostic approach. DMSA is preferred because of its lower side-effect profile. Post-provocation urinary lead levels measured within 4-6 hours more accurately reflect the body's lead burden and align better with clinical findings (16, 17).

Chelation therapy involves the use of agents such as dimercaprol (BAL), EDTA, and DMSA. DMSA is administered orally and facilitates the urinary excretion of lead. Typical regimens involve a daily dose of 10-30 mg/kg divided into three doses, followed by treatment breaks to mitigate trace element depletion. Reanalysis of post-treatment data determines the need for continued therapy (18, 19).

Case Report

This case report presents the diagnostic process, treatment, and follow-up of a 31-year-old woman diagnosed with lead toxicity, who presented to the internal medicine outpatient clinic with nonspecific but persistent complaints.

The patient's primary symptoms included chronic fatigue, dry mouth, dry eyes, polydipsia, polyuria, metallic taste, nausea, shortness of breath, impaired concentration and attention, and depressive mood. These symptoms persisted for 4-5 years, during which she reported progressive worsening despite multiple medical evaluations and treatments. Iron deficiency, vitamin deficiency, and hypothyroidism were diagnosed; however, their respective treatments failed to provide relief. Additionally, the patient pursued complementary therapies, such as phytotherapy and cupping therapy, which also yielded no improvement.

Over the past two years, the following abnormalities were consistently detected in the patient's laboratory test results:

- C-reactive protein (CRP): 3-10 mg/dL
- Erythrocyte sedimentation rate (ESR): 40-50 mm/h
- Thyroid-stimulating hormone (TSH): 8-12 mIU/L

All other laboratory parameters were within the reference range. Imaging studies, including chest radiography, thyroid ultrasonography, abdominal ultrasonography, and brain magnetic resonance imaging, showed no pathological findings to explain her symptoms.

The patient was screened for various conditions that could be associated with their complaints, including vitamin B12, vitamin D, folic acid, iron, and magnesium deficiencies, diabetes mellitus, and infectious pathologies. However, no underlying diseases were identified during these evaluations.

Given the absence of a definitive diagnosis despite extensive evaluation, heavy metal analysis was performed. The analysis was conducted at the Istanbul University Forensic Medicine and Forensic Sciences Institute, Department of Science, and Forensic Toxicology Laboratory, a specialized and accredited facility. Sample collection adhered to the laboratory's established protocol.

The patient's first urine after waking was discarded, and a 100 mL sample was collected from the second void of the day, labeled as the "pre-DMSA sample." Subsequently, a weight-based dose of 1800 mg DMSA (30 mg/kg) was administered. Urine was then collected for six hours post-DMSA administration in a designated container, with a final 100 mL sample extracted and labeled as the "post-DMSA sample." Both samples were transported in accordance with the biological material transfer protocols.

Laboratory analysis revealed that all heavy metals and trace elements, except lead, were within the reference ranges in both pre- and post-DMSA samples. However, lead levels showed a significant elevation.

- Pre-DMSA sample: 1.1 µg/g creatinine (reference range <5 µg/g creatinine)
- Post-DMSA sample: 85.3 µg/g creatinine (reference range <5 µg/g creatinine)

The approximately 80-fold increase in lead levels post-DMSA confirmed the diagnosis of lead toxicity.

The patient was initiated on a 3-month course of DMSA chelation therapy, administered at a dose of 30 mg/kg/day divided into three daily doses. The regimen included 5-day treatment cycles followed by 9-day breaks to prevent the depletion of essential minerals and trace elements. Routine clinical evaluations and laboratory monitoring were performed throughout the treatment period. No adverse effects or complications were observed.

At the end of the 3-month therapy, repeat testing was conducted using the same collection and analysis protocols. The results demonstrated a marked reduction in the lead levels.

- Pre-DMSA sample: 0.2 µg/g creatinine (reference range <5 µg/g creatinine)
- Post-DMSA sample: 11.3 µg/g creatinine (reference range <5 µg/g creatinine)

Pre- and post-treatment urine lead levels are schematically represented in Figures 1 and 2. The significant decrease in lead levels post-treatment correlated with clinical improvement, including a reduction in the patient's primary symptoms.

A graphical illustration of the study is shown in Figure 3.

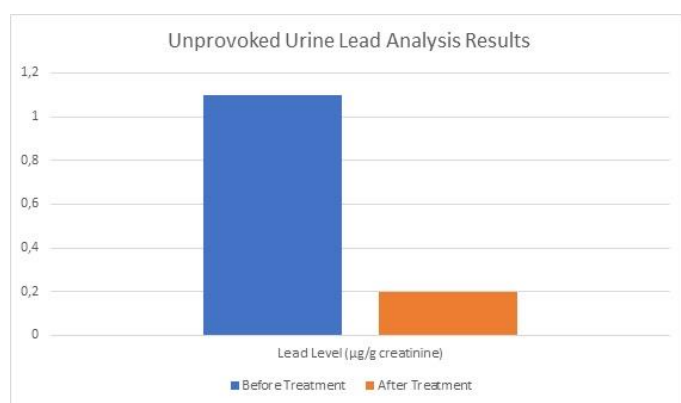


Figure 1. Unprovoked urine lead analysis results of the case before and after treatment.

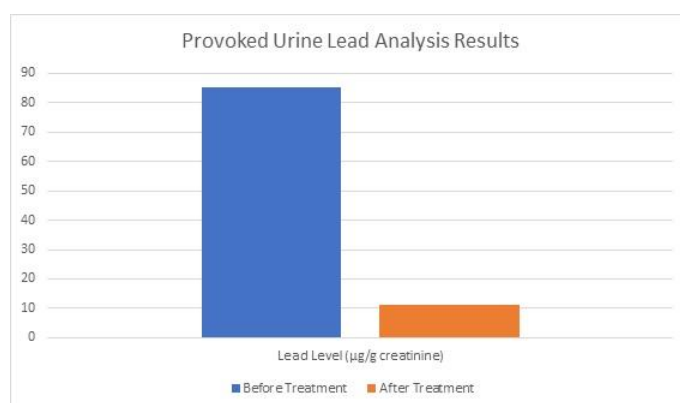


Figure 2. Provocative urine lead analysis results of the case before and after treatment.

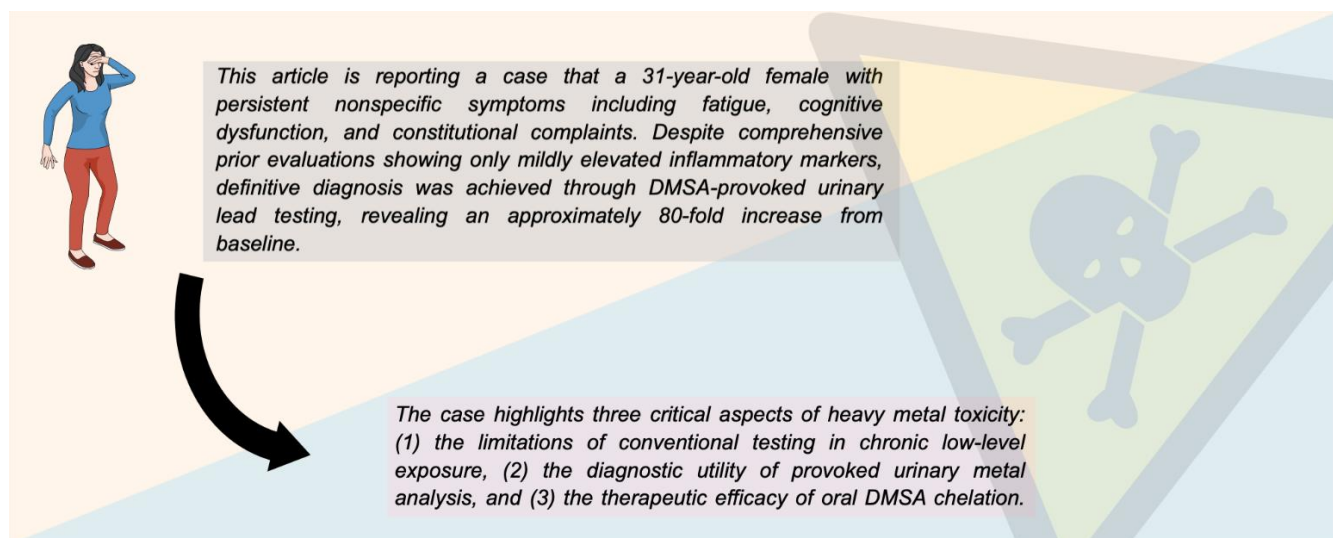


Figure 3. Graphical illustration of the study.

Discussion

Government regulations and inspections have led to a significant reduction in heavy metal exposure compared to previous decades, making severe cases increasingly rare. However, chronic and low-dose exposures, similar to the case we presented, remain a significant concern. These exposures often manifest with nonspecific symptoms, complicating routine clinical evaluations and delaying the consideration of heavy metal toxicity as a potential diagnosis. Additionally, standard blood and urine analyses frequently fail to reflect the true toxic burden, further complicating the diagnostic efforts. Consequently, patients with such exposures often consult multiple physicians, undergo numerous tests, and receive treatments without definitive results (7-11).

The presence of heavy metal levels within the reference range in routine analyses does not eliminate the possibility of toxicity. For patients with a clinical suspicion of heavy metal exposure, advanced diagnostic techniques involving the use of chelation agents are critical. These agents mobilize metals from tissues, facilitating their excretion in the urine for analysis. Among these, dimercaptosuccinic acid (DMSA) is particularly advantageous because of its oral administration, widespread use, and relatively favorable side effect profile (16, 17).

Comparative analyses of pre- and post-provocation urine samples provide valuable insights into the degree of metal toxicity. In the present case, an approximately 80-fold increase in lead levels following provocation indicated significant exposure. Furthermore, the effectiveness of the treatment can be assessed by repeating these post-treatment measurements. Chelation therapy involves the use of agents such as dimercaprol (BAL), EDTA, and DMSA. However, BAL and EDTA have relatively broader side effect profiles and require a more complex administration process than DMSA; therefore, they are not first-line treatment options (20, 21). In our patient, a three-month course of DMSA chelation therapy resulted in a 7- to 8-fold reduction in both pre- and post-provocation lead levels. This reduction was consistent with clinical improvements and other laboratory findings, confirming the success of the intervention.

The reference value for post-provocation measurements is often cited as $<5 \mu\text{g/g}$ creatinine in the laboratory guidelines. However, this threshold may not adequately account for the variability in provoked measurements. A study from Belgium suggested setting the upper limit at $22 \mu\text{g/g}$ creatinine for lead levels post-DMSA provocation (17). In our case, the pre-treatment values exceeded this proposed upper limit, whereas the post-treatment values were markedly below it, providing further evidence of therapeutic efficacy.

This case underscores the importance of considering advanced diagnostic approaches in cases of suspected chronic heavy metal exposure and highlights the utility of DMSA as both a diagnostic and therapeutic tool.

Conclusion

Heavy metal toxicity should be considered in patients with nonspecific symptoms that are unresponsive to conventional treatments. Advanced diagnostic methods and chelation therapy play pivotal roles in the management of this condition. Collaboration with experienced laboratories ensures accurate analysis and optimal patient outcomes.

Disclosures

Informed Consent: Written informed consent was obtained from the patient.

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Author Contributions: Concept - İ.B.; Design - İ.B.; Supervision - İ.B.; Materials - İ.B.; Data collection &/or processing - İ.B.; Analysis and/or interpretation - İ.B.; Literature search - İ.B.; Writing - İ.B.; Critical review - İ.B.

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